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EDITORIAL COMMENT

Atherosclerotic plaque imaging by PET/CT; can inactive, active and mixed plaques be discerned?

E. E. van der Wall · J. D. Schuijf · J. W. Jukema · J. J. Bax · A. van der Laarse

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Atherosclerosis is one of the leading causes of morbidity and mortality in the world. Rupture of atherosclerotic plaques and formation of thrombi are the primary mechanisms of myocardial infarction or cerebrovascular accidents. Atherosclerosis is therefore a dynamic inflammatory disorder and the biological composition and inflammatory state of an atherosclerotic plaque, rather than the degree of stenosis or its size, are the major determinants of acute clinical events [1, 2]. Noninvasive techniques to detect vulnerable atherosclerotic plaque are critically needed. In recent years, radionuclide imaging [3–6], magnetic resonance imaging (MRI) [7–13], and computed tomography (CT) have been put forward as the most relevant imaging modalities to identify atherosclerotic vascular disease and the vulnerable plaque [14–30]. Positron emission tomography with fluorodeoxyglucose (FDG-PET) has become one of the advanced imaging approaches for the detection of vulnerable plaques [31]. Ogawa et al. [32] showed that macrophages are responsible for the accumulation of FDG in atherosclerotic lesions whereby FDG uptake is correlated with macrophage density. Because vulnerable plaques are rich in macrophages, FDG imaging should be useful for selective detection of such plaques. In recent years, multislice CT has been shown to provide excellent anatomical and morphological images both of the large vessels and the coronary arteries [18]. In addition, differences in plaque composition and distribution—both in acute coronary syndromes and stable coronary artery disease—can adequately be visualized with multislice-CT [29, 30].

Hybrid imaging with both PET and CT, being a combined functional and structural whole-body imaging modality, could therefore offer the optimal potential to characterize plaque composition [33, 34]. Tatsumi et al. [35] showed in 85 patients who underwent FDG PET/CT imaging that FDG uptake was commonly depicted in the thoracic aortic wall. The FDG uptake site was mostly distinct from the calcification site and was located in areas of metabolic activity (i.e., macrophages) of atherosclerotic changes. Ben-Haim et al. [36] evaluated FDG uptake in atherosclerotic plaques in 50 asymptomatic patients. Repeat PET/CT studies were performed to assess changes in patterns of FDG uptake and CT calcifications. FDG-avid foci represent a dynamic process of transient inflammation, whereas CT calcifications indicate stable atherosclerosis. Hybrid imaging with PET/CT creates therefore incremental value over both imaging modalities alone. Rudd et al. [37] showed that atherosclerosis imaging with FDG-PET/CT was useful for tracking inflammation within plaques.

Editorial comment to the paper by Wassélius et al. (DOI:10.1007/s10554-008-9366-5).

E. E. van der Wall (✉) · J. D. Schuijf · J. W. Jukema · J. J. Bax · A. van der Laarse
Department of Cardiology, Leiden University Medical Center, Albinusdreef 2, 2333-ZA Leiden, The Netherlands
e-mail: E.E.van_der_Wall@lumc.nl

The authors assessed the short-term reproducibility of PET/CT in peripheral artery disease. Twenty patients with vascular disease underwent PET/CT imaging of the iliac, femoral, and carotid arteries 90 min after FDG administration. Mean and maximum target-to-background ratios in the carotid, iliac, and femoral arteries were highly reproducible. It was suggested that mean target-to-background ratio could be used for tracking systemic arterial therapies, whereas the maximum target-to-background ratio proved to be optimal for detecting and monitoring local, plaque-based therapy.

In the present issue of the *International Journal of Cardiovascular Imaging*, Wasselius et al. [38] assessed atherosclerotic plaques in a large asymptomatic population stratified to age and sex. The authors analyzed 200 patients in four age-groups of 20–30, 40–50, 60–70 and 80–90 years old, who were referred for whole-body FDG-PET/CT-examination. Uptake of FDG in active, calcified inactive and mixed atherosclerotic plaques was assessed in eight defined vessel segments. There was a high correlation between the total number of cardiovascular risk factors and the number of FDG-accumulating active plaques as well as the number of CT-determined calcified inactive plaques. A significant difference in the number of plaques between all age-groups was observed except for active plaques in the age groups of 60–70 and 80–90 years. A remarkable finding was that mixed plaques were very rare, similar to previous findings [39], suggesting that plaque inflammation and calcification are indeed discrete temporal pathophysiological entities. In addition, high counts for active plaques generally were paralleled by high counts for inactive, calcified plaques. Furthermore, a decrease in the number of active plaques was also accompanied by decreases in inactive, calcified plaques. This finding suggests that the lesions detected in the walls of large arteries by FDG-PET represent inflammation associated with the early phases of atherosclerosis. Lastly, statin-treatment was associated with a significantly lower number of active plaques. Consequently, FDG-PET/CT imaging was able to assess total plaque burden of patients, to identify plaque composition, and to monitor medical treatment of inflamed atherosclerotic plaques.

In a recent study by the same group [40], it was shown that graft infection was a serious complication to vascular surgery. FDG uptake was assessed in vascular grafts in 2,045 patients with or without symptoms of graft infection. Of all 2,045 patients examined by PET/CT, 16 patients with synthetic aortic grafts were identified and reevaluated for FDG accumulation. High FDG uptake was found in 10 of 12 grafts in the patients who underwent open surgery and in one of four grafts in patients who underwent endovascular aneurysm repair. Uptake of FDG in vascular grafts was found in the vast majority of patients without graft infection, even a long time after surgery. The basis for the FDG accumulation could be the chronic inflammation known to occur on the surface of synthetic graft material. Accumulation of FDG appeared to be less prominent in endovascular grafts than in conventional grafts.

In summary, integrated PET/CT imaging is a powerful new noninvasive modality that offers the potential for refined diagnosis and management of the entire spectrum of cardiovascular atherosclerosis [41]. Using PET/CT imaging, plaque inflammation (active plaques) and calcification (inactive plaques) can be observed as discrete temporal pathophysiological entities. Combined PET/CT imaging may therefore be superior to the single use of both PET imaging and CT angiography in guiding pharmacological treatment, assisting in revascularization decisions, and evaluating therapeutic effects.

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